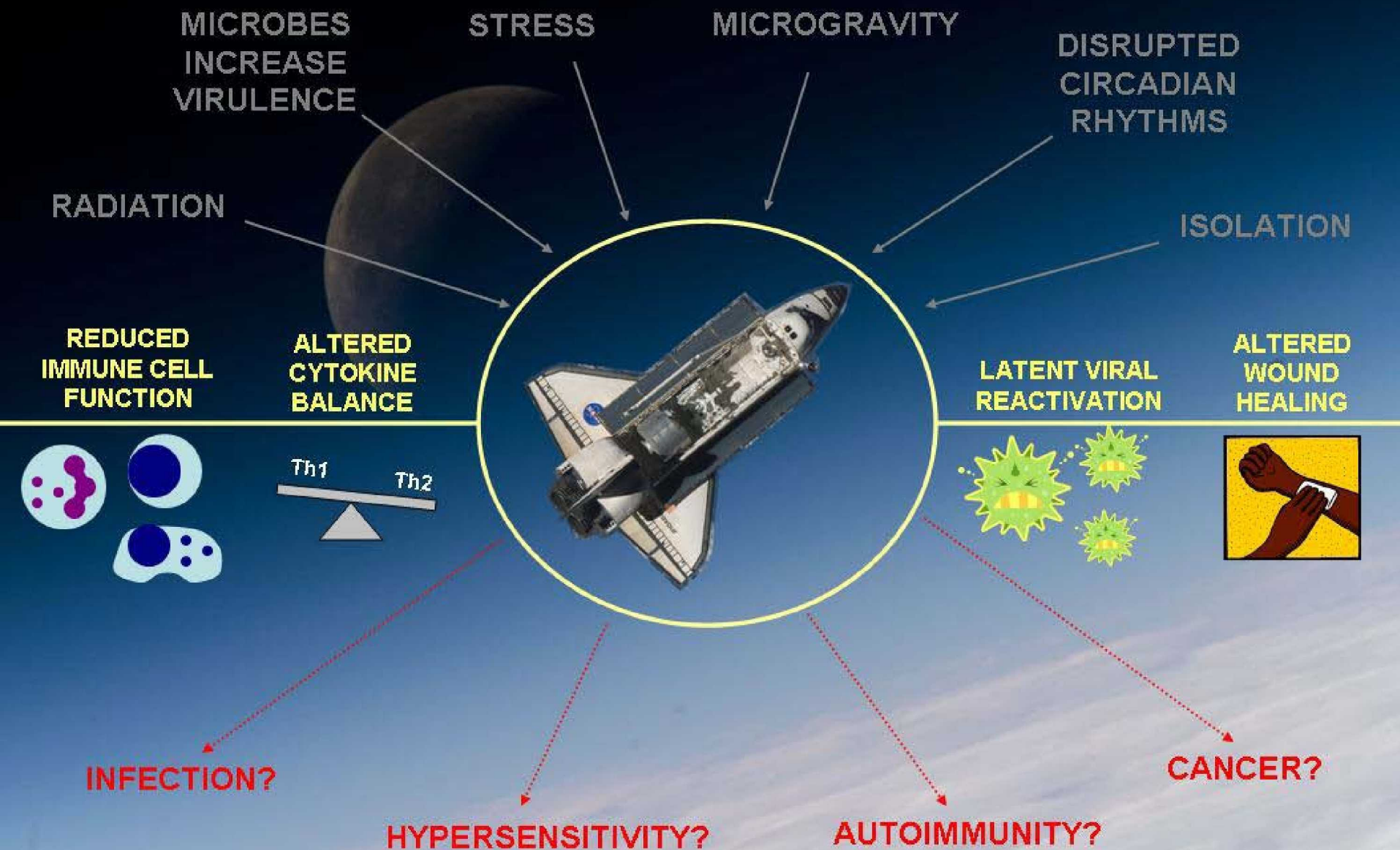


CONCORDIA STATION, DOME C, ANTARCTICA AS A GROUND-BASED ANALOG FOR  
SPACEFLIGHT/PLANETARY EXPLORATION

**Consequences of Longterm-Confinement and Hypobaric Hypoxia on  
Immunity in the Antarctic Concordia Environment  
(ESA - CHOICE Study)**

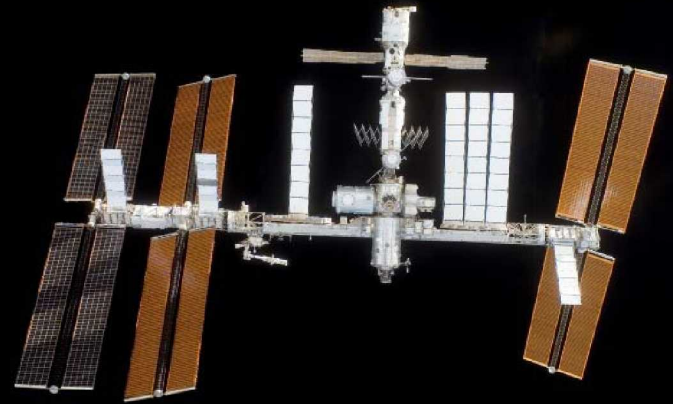
Brian Crucian, Alexander Chouker, Duane Pierson, Satish Mehta, Raymond Stowe, Alex Salam and Clarence Sams

# Spaceflight-associated immune dysregulation



# Human Research Program Requirements Document

**Baseline May 2007**



HRP Element: HHC

**Risk: Crew Adverse Health Event Due To Altered Immune Response**

Human immune function is altered in- and post-flight, but it is unclear if this change leads to an increased susceptibility to disease. Reactivation of latent viruses has been documented in crewmembers, though this reactivation has not been directly correlated with the immune changes nor with observed disease. Further research may elucidate whether microgravity exposure impairs the immune system, and whether this change represents a health risk to crews.

# SAT Report, Immune-related Knowledge Gaps

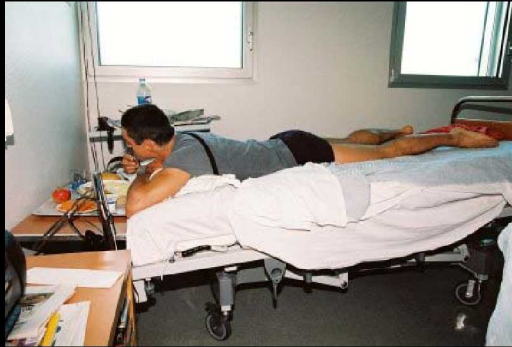
- IM1** Lack of in-flight immune data. In-flight data required to determine risk.
- Formulation of an improved immunology standard for exploration spaceflight.
- IM2** This is not a research gap, but will be derived from the filling of gap: Lack of in-flight immune data. In-flight data required to determine risk.
- IM3** Lack of ground analog studies. Suitable ground analogs for immune dysregulation have been identified. Forward work may be expedited using these opportunities.\*\*
- IM4** Lack of in-flight hardware to evaluate hematology /infection/immunity. Capability must be developed prior to exploration missions.
- IM5** Investigation of individual records of in-flight illness for clarification of time course/etiology.

\*\*Specific directive from program review: evaluate Antarctica winter-over as potential analog for SAID.



# (Human) Ground-based Space Flight Analogs

**Extended head-down bed rest**



**MARS-500 (IBMP – Moscow)**



**Closed Chamber Confinement**



**NEEMO Aquarius Station**



**Haughton-Mars Project**



**Antarctica winter over**



## Best Analogs for SAID

An analog which simulates (or actual) mission-deployment, associated risk, adverse environment, isolation, psychological/physiological stress, disrupted circadian rhythms, etc.

# Immunology Flight Studies





ANNOUNCEMENT OF OPPORTUNITY  
FOR MEDICAL, PHYSIOLOGICAL AND PSYCHOLOGICAL RESEARCH  
USING THE CONCORDIA ANTARCTIC STATION

Consequences of longterm-*Confinement* and *Hypobaric*  
*HypOxia* on *Immunity* in the antarctic *Concordia*  
*Environment* (*CHOICE* – Study)

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Crucian, Brian (STM, Co-I); Johnson Space Center (JSC), NASA, USA

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Schelling, Gustav (STM, Co-I); Ludwig-Maximilians-University of Munich, Germany

Thiel Manfred (STM, S-I), Ludwig-Maximilians-University of Munich, Germany

## 2008- New Proposal

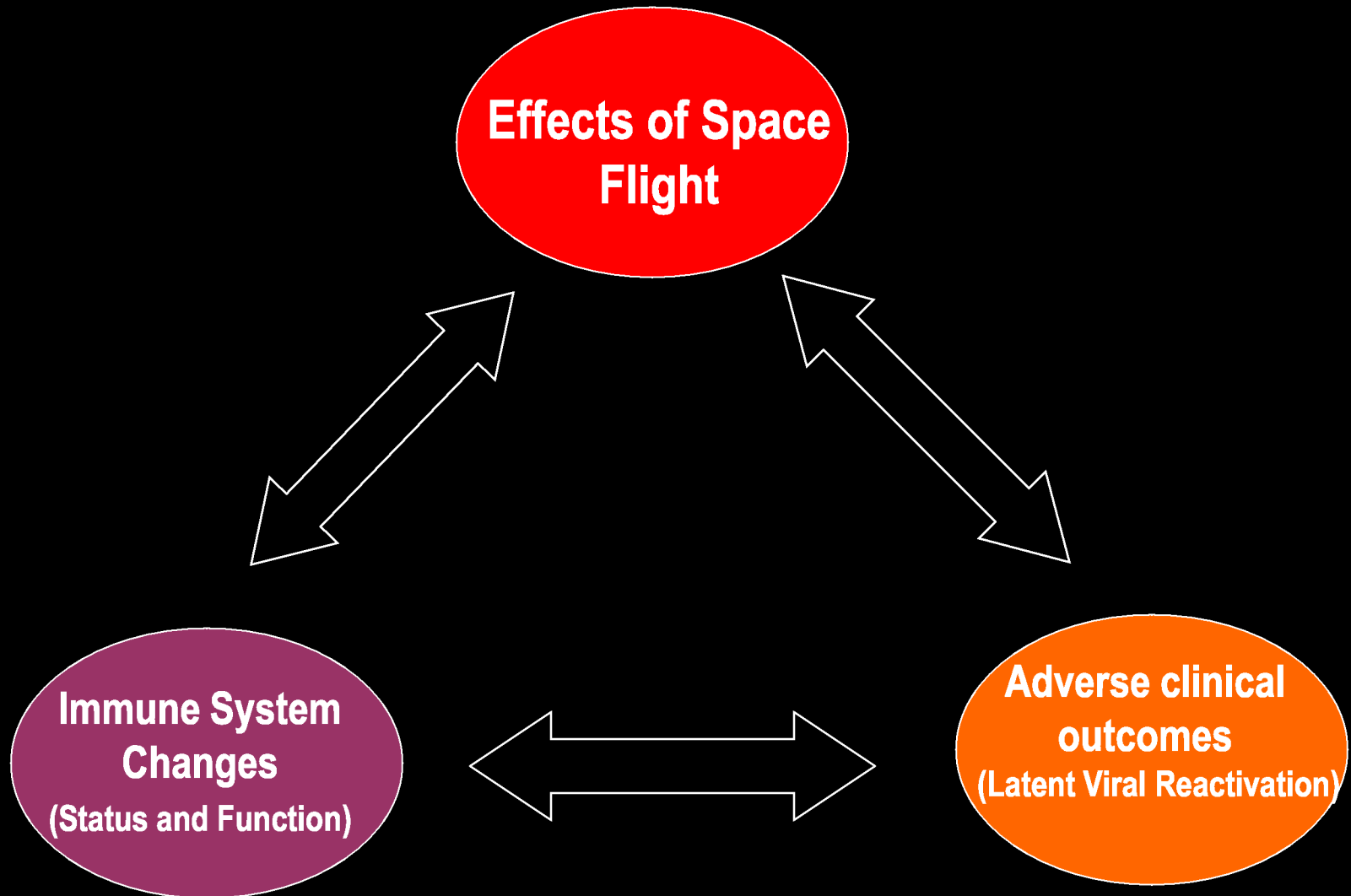


## ESA CHOICE Assays

- PMN number, function, bactericidal
- In-vitro DTH
- Apoptosis/necrosis
- Cellular mRNA expression
- Plasma purine markers of inflammation/hypoxia
- Erythropoietin activity
- Stress test
- Stress hormones
- Components of exhaled air



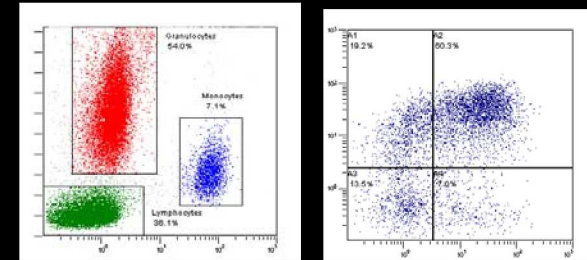
## NASA Paradigm



# NASA Integrated Immune Assays

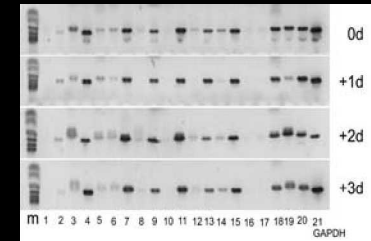
## JSC Immunology Laboratory

- Leukocyte subsets
- T cell function
- Intracellular/secreted cytokine profiles



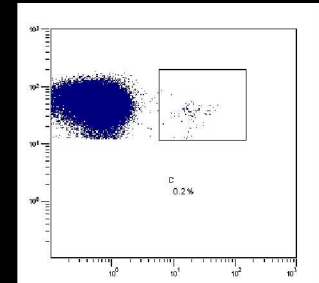
## Mercer University

- Plasma cytokine balance
- Leukocyte cytokine RNA



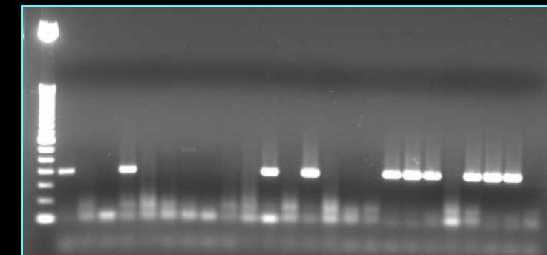
## Microgen Laboratories

- Virus specific T cell number
- Virus specific T cell function
- Plasma stress hormones

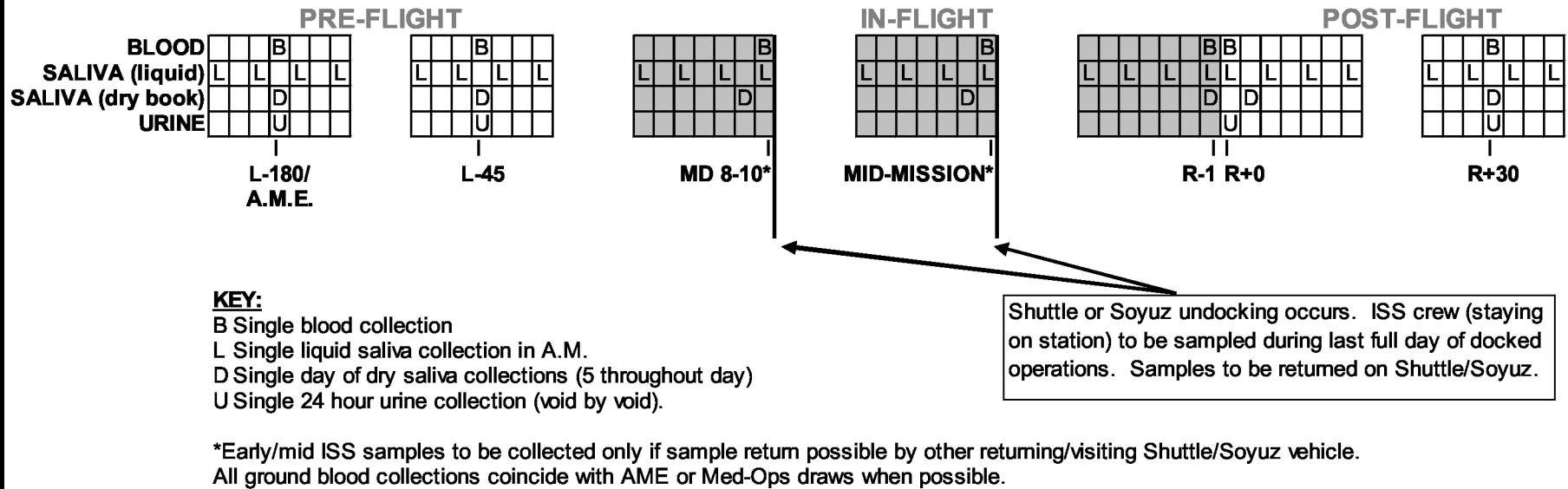


## JSC Microbiology Laboratory

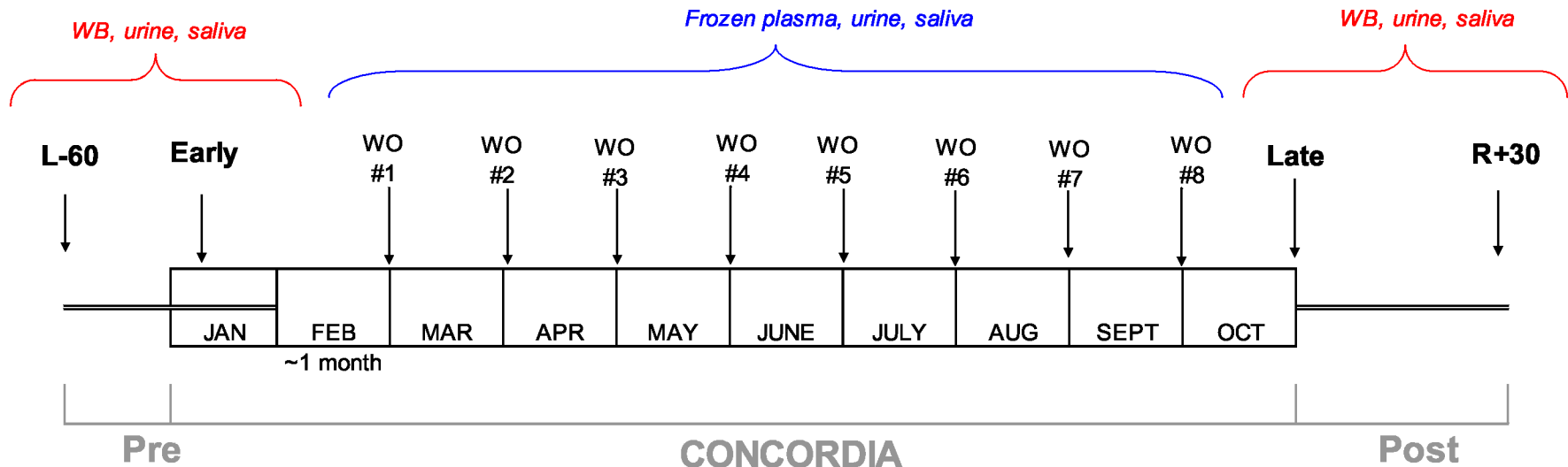
- Latent herpesvirus reactivation (saliva/urine)
- Saliva/urine stress hormones
- Circadian rhythm analysis



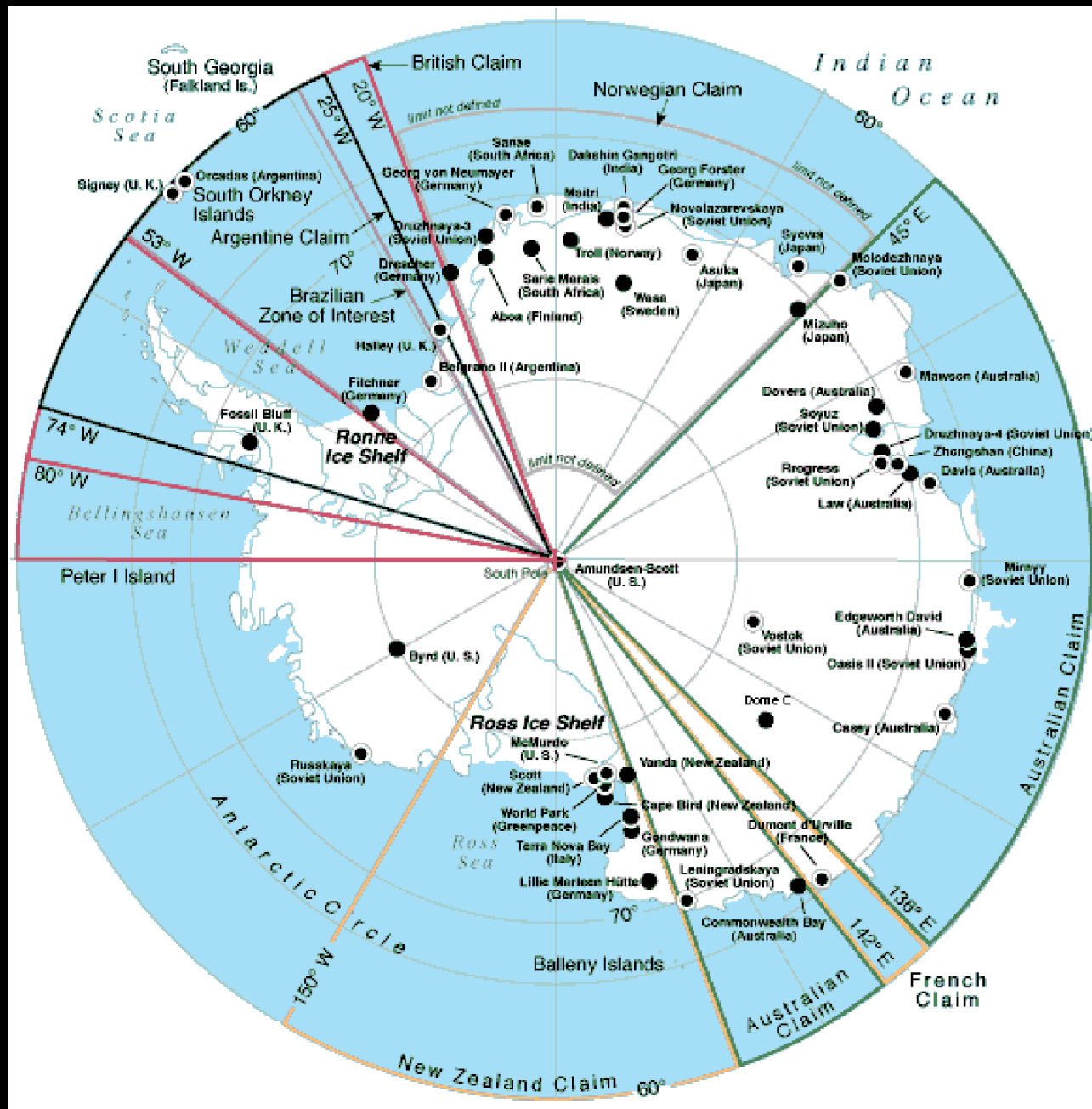
# INTEGRATED IMMUNE



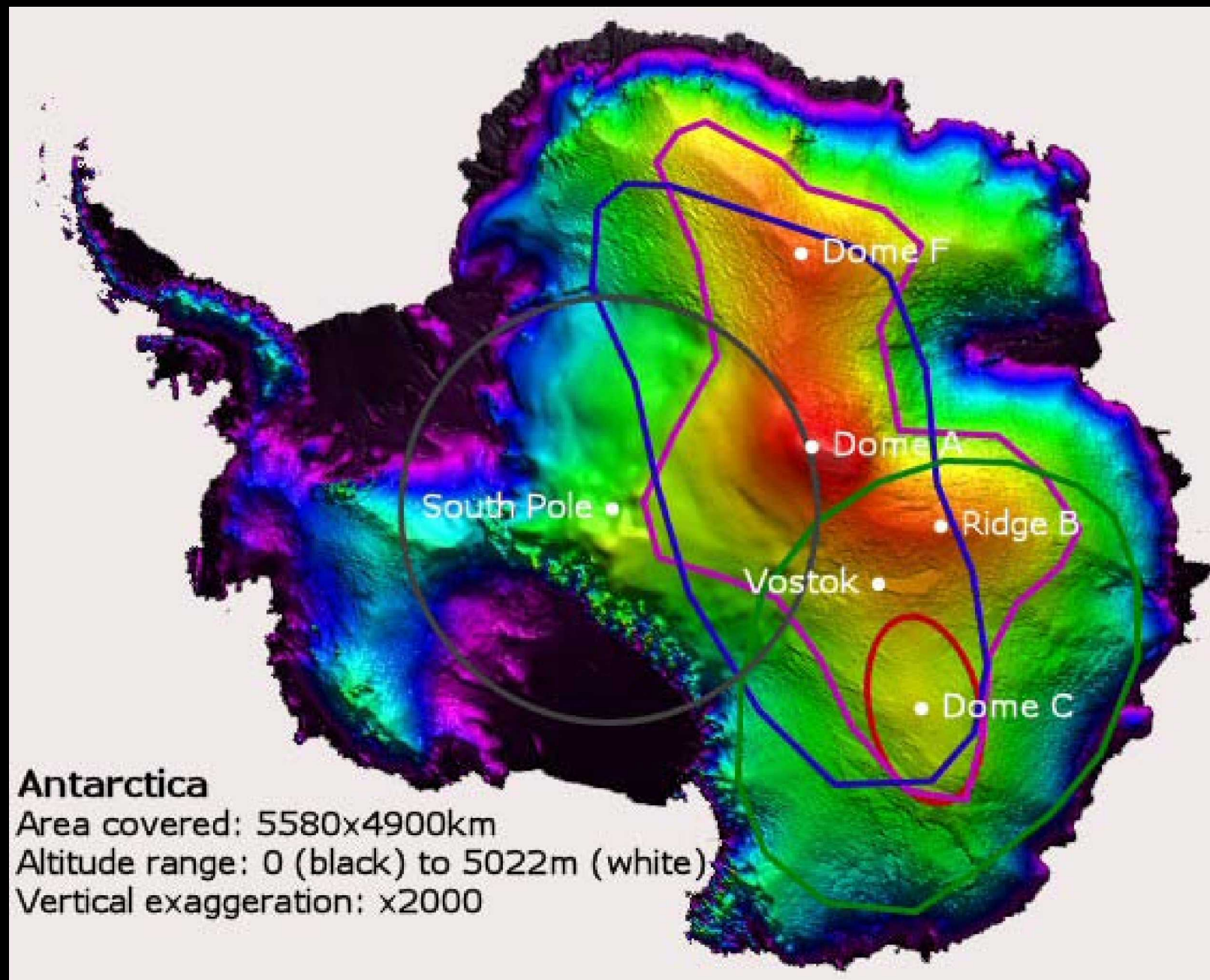
## CHOICE



# ALL ANTARCTIC STATIONS ARE NOT THE SAME...







## THE CONCORDIA ENVIRONMENT

Difficult travel in/out

Extreme isolation, even greater than ISS

Altitude 3200m (10,500 ft)

Air pressure 645hPa (mbar)

12-13 Vol% of O<sub>2</sub>

Lack of CO<sub>2</sub> in air

Higher ionization in air (increases oxidative metabolism)

*chronic hypobaric hypoxia*

- Relative humidity 3-5%
- Snowfall ~1cm/yr
- High winds
- Elevated UV exposure (summer), UV deficiency (winter)
- Mean winter temperature -60 C (-72 F)
- Mean summer temperature -30 C (-22 F)
- Disrupted circadian rhythms.

# HUMAN FACTORS

- Isolation, confinement for prolonged duration
- Limited communication capability
- International crew, multiple languages
- Sleep/wake cycles disrupted
- Actual deployment w/ associated risks
- Winter over crew: 12
- Summer crew: ~50





## Summer Transition period – Incidence Rates

(mid-November to mid-January)

- Approx. 50% of summer participants contacted infectious disease

- Historically, extremely high incidence rate

- Three periods of epidemic viral infections:

Period 1: Flu-like (mid-Nov. to mid-Dec.)

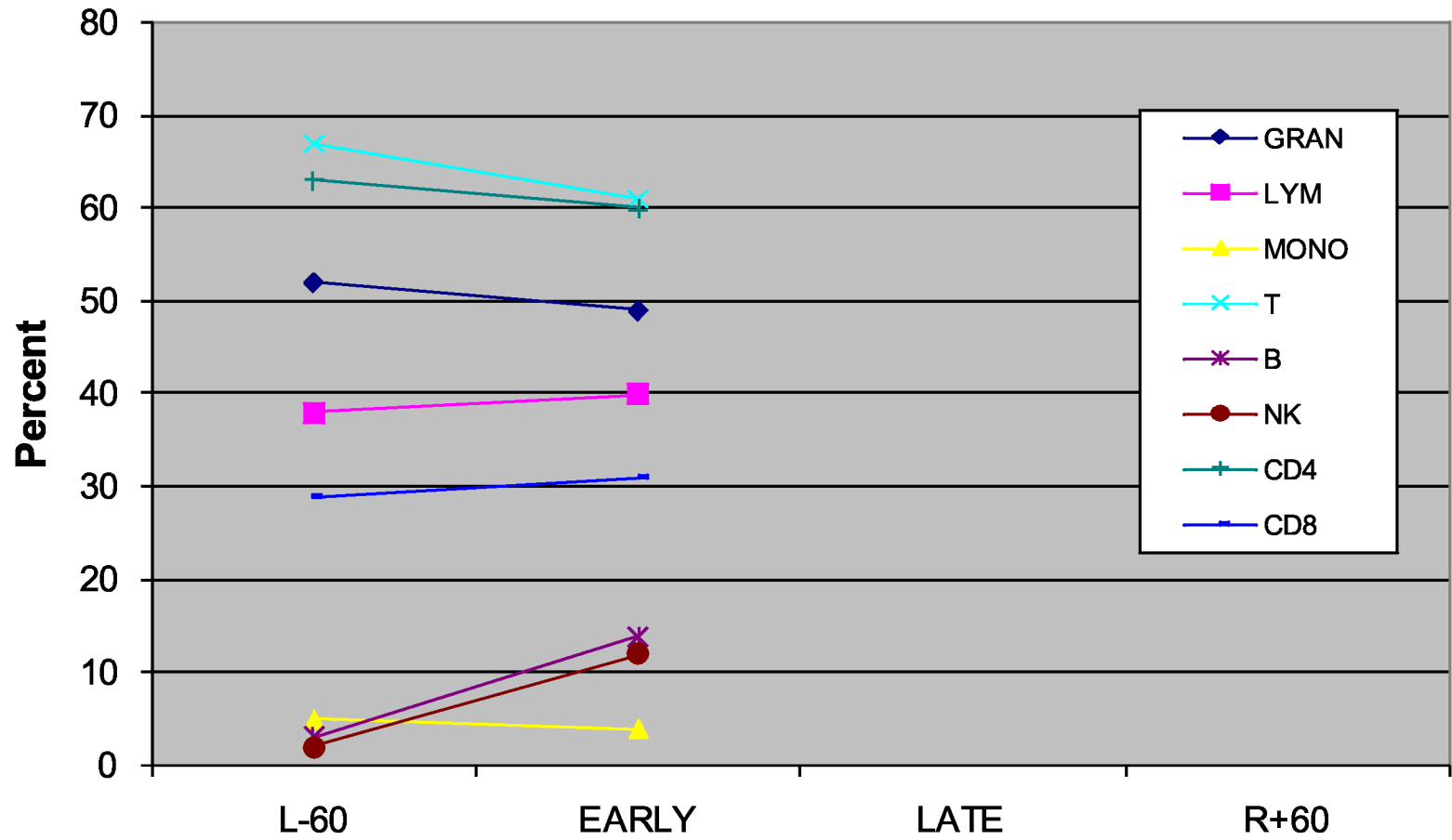
Period 2: Rhinoparyngitis (mid-Dec. to early Jan.)

Period 3: Gastro-enteritis (late-Dec. to early Jan.)

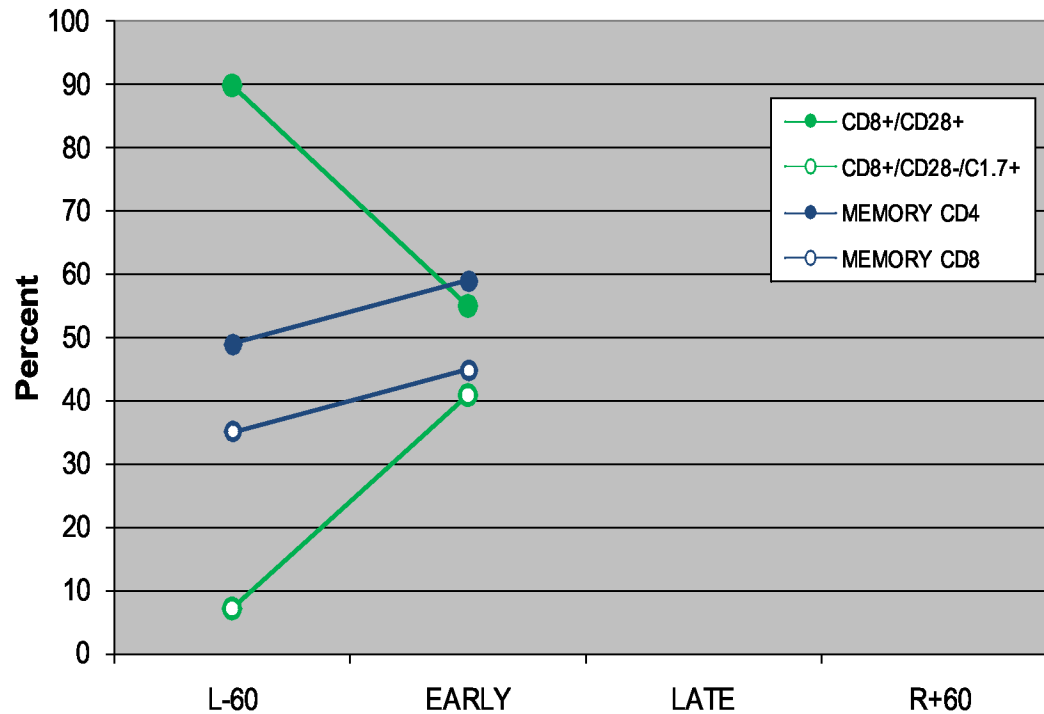
# NASA CHOICE Assays

<b>BLOOD ASSAYS</b>	<b>Pre, post sampling</b>	<b>In- sampling</b>	<b>Details</b>	<b>NASA Lab</b>
Comprehensive immunophenotype	WB		(see panel)	Immune
Intracellular cytokine profiles (T cell)	WB		PMA+ION, LPS	Immune
T cell function	WB		CD3/CD28, A+B	Immune
Secreted cytokine profiles	WB		Th1/Th2, Inflam.	Immune
Viral DNA - PBMC	WB		EBV	Mcgn
Circulating viral-specific T cells	WB		EBV, CMV	Mcgn
Viral-specific T cell function	WB		EBV, CMV	Mcgn
Viral antibodies titers	Plasma	Plasma	EBV, CMV	Mcgn
Viral antibodies titers	Plasma	Plasma	VZV	Micro
Plasma stress hormones	Plasma	Plasma	cortisol	Mcgn
<b>SALIVA ASSAYS</b>				
Saliva stress hormones, Diurnal	Dry Saliva	Dry Saliva	cortisol, DHEA	Micro
Viral DNA by PCR	Liquid Saliva	Liquid Saliva	CMV*, EBV, VZV	Micro
<b>URINE ASSAYS</b>				
Viral DNA by PCR	24hr. URINE	24hr. URINE	CMV	Micro
Urine stress hormones	24hr. URINE	24hr. URINE	cortisol*, cat.*	Micro

# LYMPHOCYTE SUBSETS



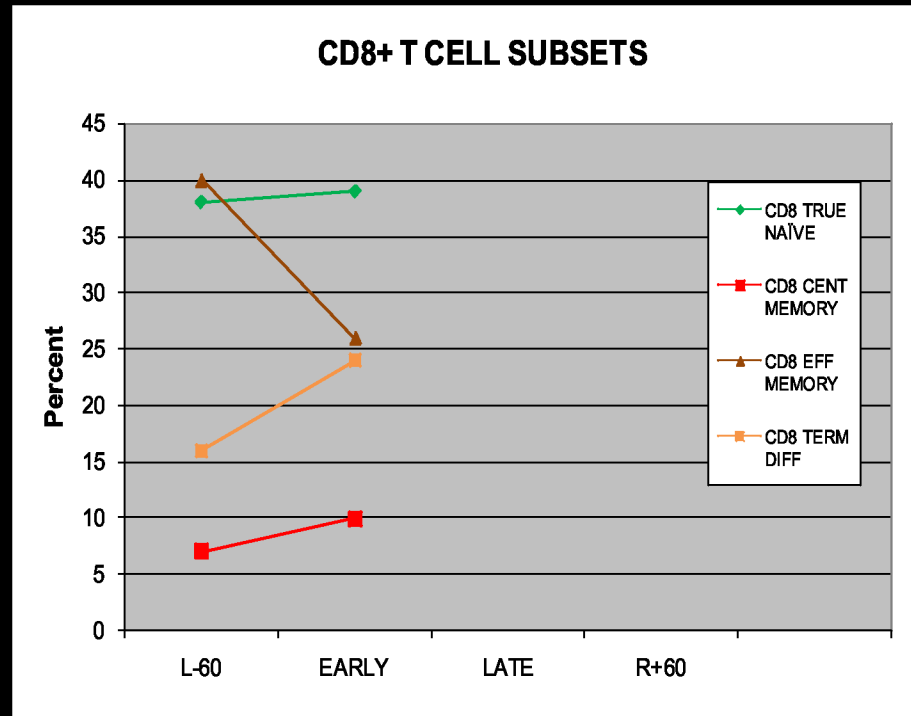
## MEMORY/NAIVE T CELL SUBSETS



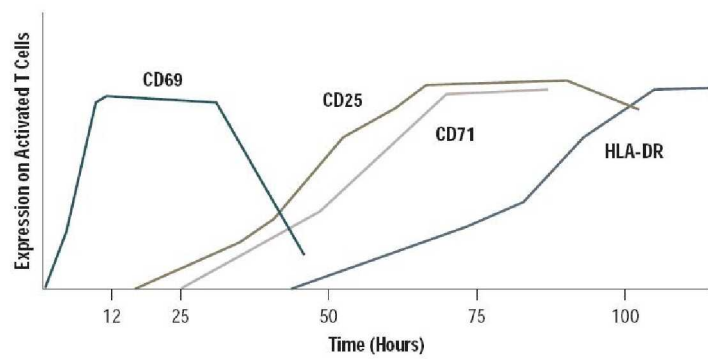
Increase in memory CD4, memory CD8 during deployment. Similar to flight crew, reflects immune activation.

Shift among CD8 subsets, increases in late activation, senescent subsets, reflective of chronic activation.



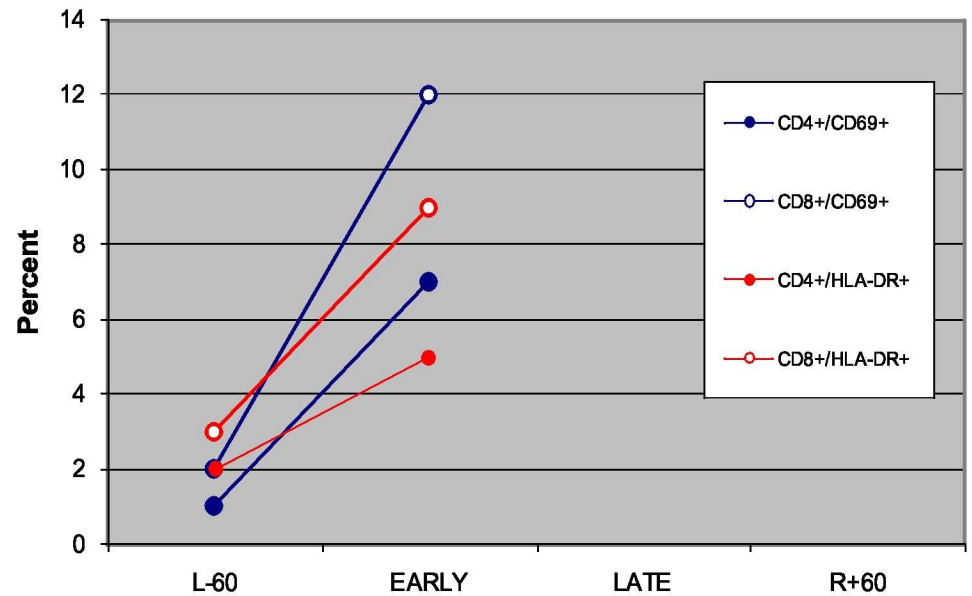


Increase in terminally differentiated memory CD8, also reflective of chronic activation, corresponding decrease in the effector memory subsets.



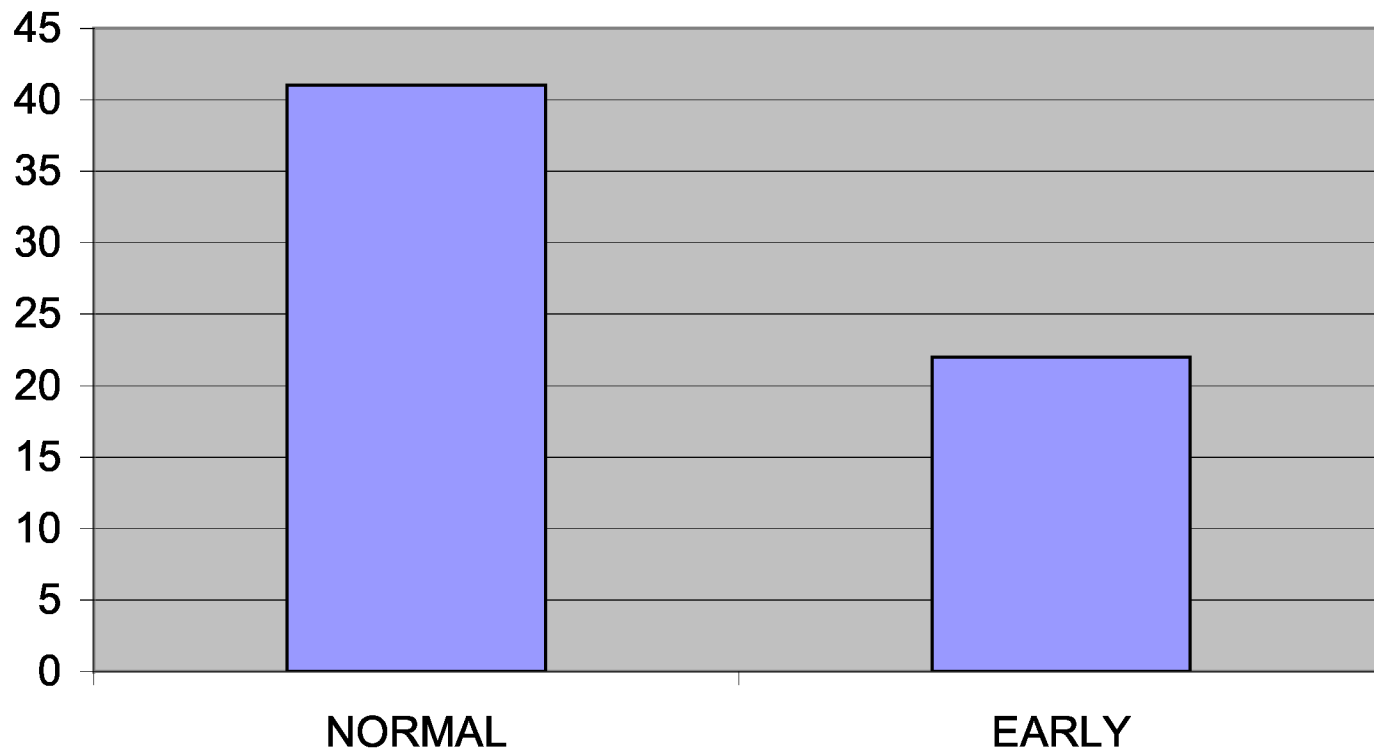
Kinetics of Expression of Activation Antigens on T Cells

## ACTIVATED T CELL SUBSETS

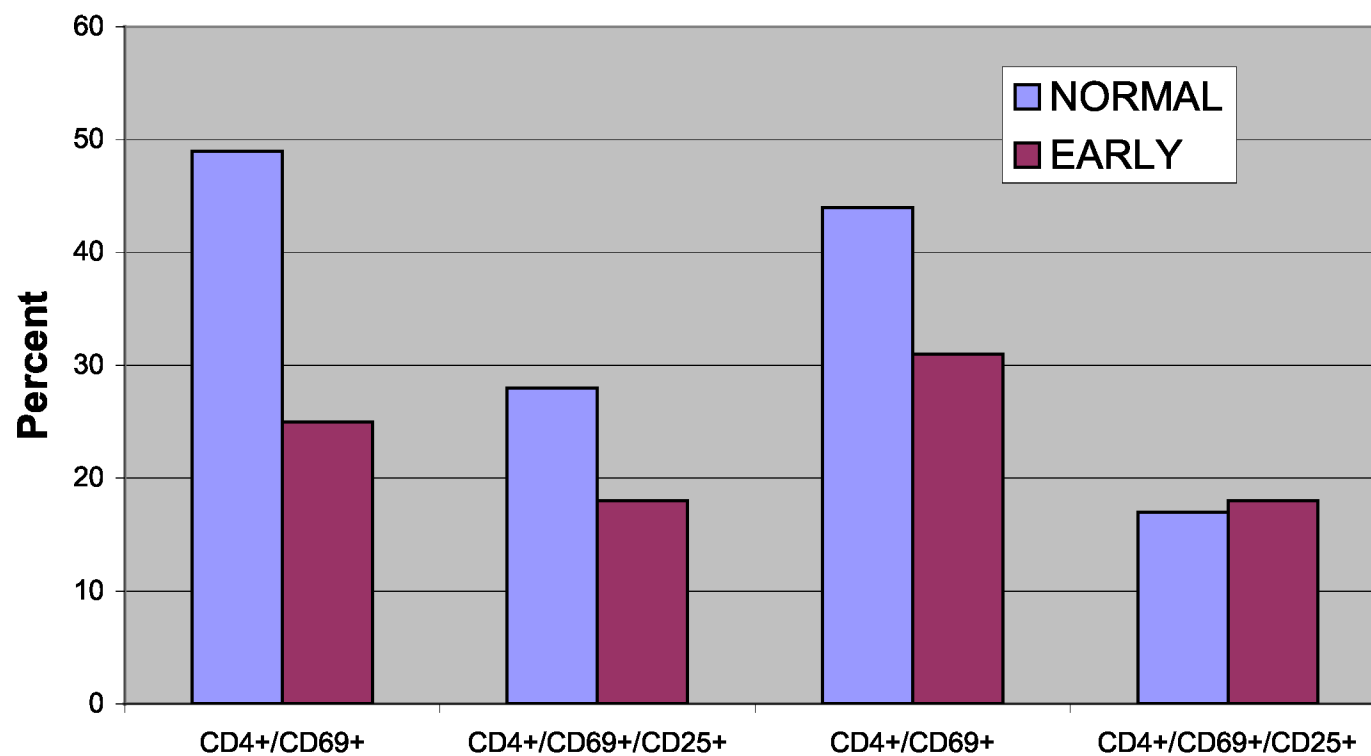


Increases in constitutively activated CD4+ and CD8+ T cells

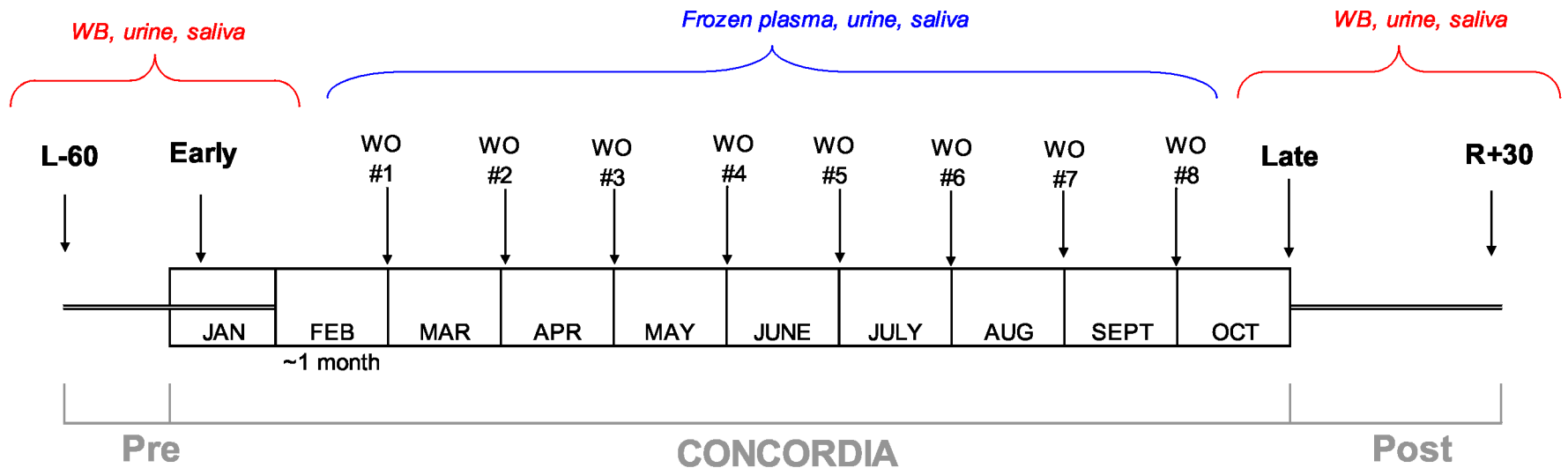
# CD8+/IFN $\gamma$ +



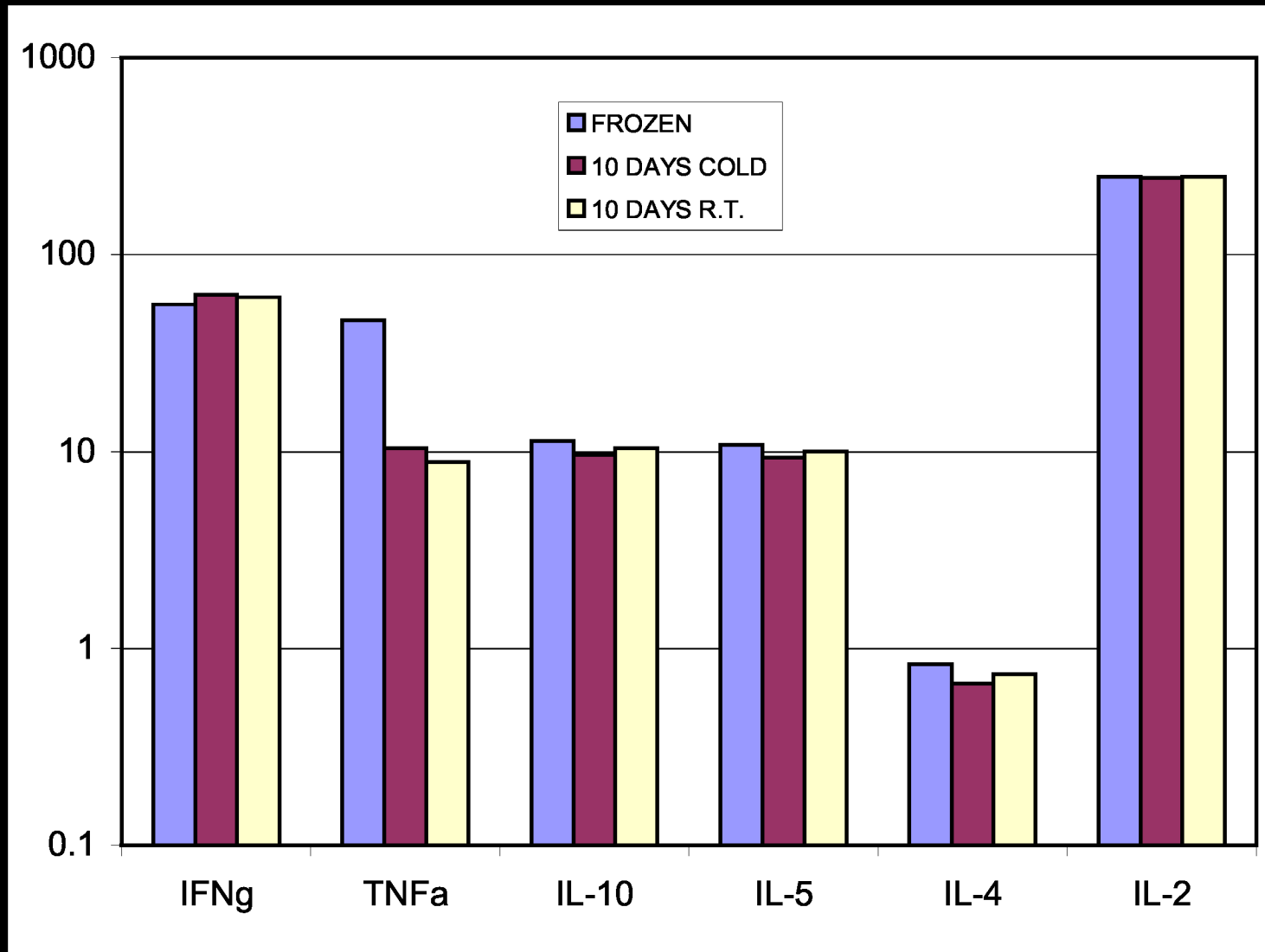
## T Cell Function - A+B 24hr Culture



# CBA Assay: secreted cytokine profiles

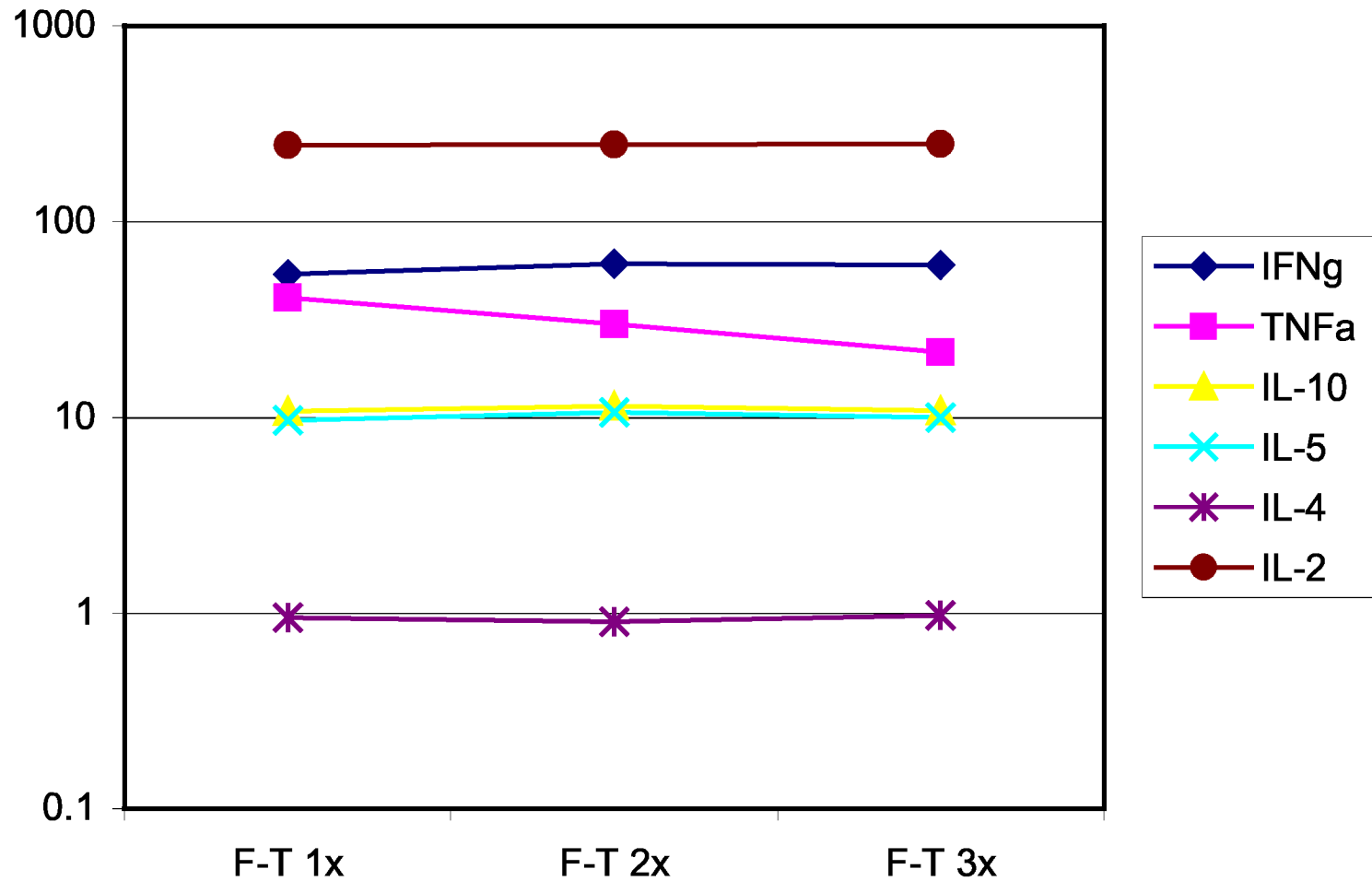


## Secreted cytokine culture supernatants: 10 day RT stability





## Secreted cytokine culture supernatants: multiple freeze-thaw

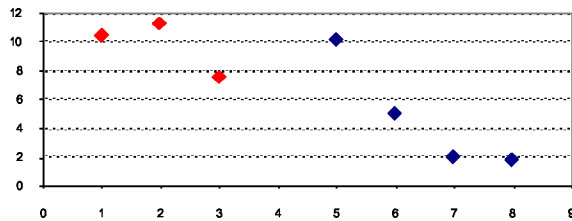


# CBA Assay: secreted cytokine profiles

3 TCR 'responder CHOICE subjects; 4 control subjects

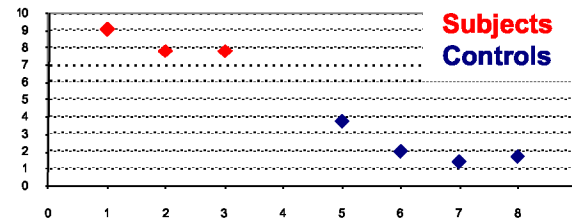
CD3/CD28 – 48hr

IL-10



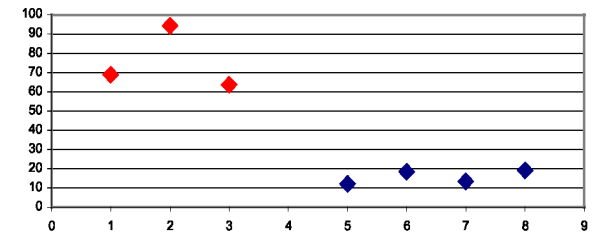
PMA/I – 48hr

IL-10

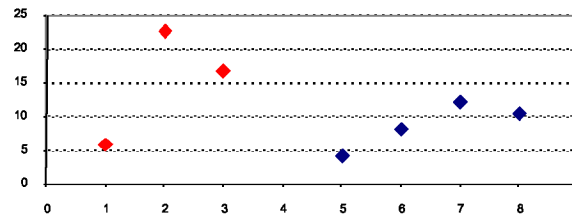


LPS – 48hr

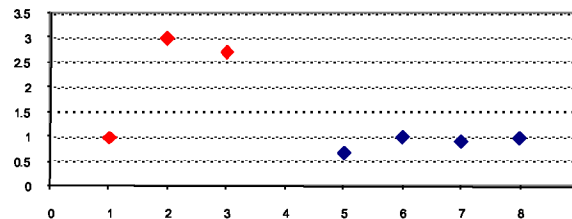
IL-1b



IL-5



IL-4



## Unplanned 'bonus' mid-winter testing

- Partec cytometer plan: bring in/out for support of each early/late timepoint.
- Revised to leave during winter over, with Dr. Salam to process samples.
- Reagents issues
- Consumable supply issues
- Data/training issues
- Additional assays as training/reagents/consumables allowed, phenotype, cell cultures.
- First run: deployment month #2. Samples collected at DC, data acquired at DC, data emailed to JSC, analysis performed at JSC.

